PATENT COOPERATION TREATY

PCT

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2005/000443	13.01.2005	16.01.2004

International Patent Classification (IPC) or both national classification and IPC
C12N15/85, A61K39/00, A61K48/00

Applicant
GLAXO GROUP LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/000443

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/000443

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 19,21 (industrial applicability)

because:

☒ the said international application, or the said claims Nos. 19,21 (industrial applicability) relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/000443

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1-5,7-13,15,20,21
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-23
Industrial applicability (IA)	Yes:	Claims	1-18,20,22,23
	No:	Claims	

2. Citations and explanations

see separate sheet

I. Basis (Continuation)

The statement that the written and electronic sequence listings subsequently filed to this I.S.A. do not include matter which extend beyond the content of the application as filed is missing. Since it is a legal requirement, the sequence listings might be considered as not having been validly filed.

III. Non-establishment of opinion (Continuation)

Claim 19, and claim 21 as far as the latter relates to a method practised in vivo, relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated in respect of the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

V. Reasoned statement (Continuation)

1. CITATIONS

Reference is made to the following documents:

D1: Chan Y-J et al (1996) J.Virol. vol.70, pp.5312-5328.

D2: WO0236792 (Glaxo Group Limited; Catchpole, Ian, Richard; Ellis Jonathan, Henry) 10 May 2002 (2005-05-10).

2. NOVELTY (Art. 33(2) PCT)

2.1. The present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of claims 1-5,7-13,15,20 and 21 is not new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT): D1 discloses the functional characterisation of hCMV's US3 transcriptional regulatory elements and identifies a.o. Repressor, Enhancer and minimal promoter elements. D1 notably describes the preparation of polynucleotide vectors comprising the US3 enhancer in combination with the US3 minimal promoter and a heterologous gene (E/IES-CAT: p.5315 col.2 par.2; E/IES-Luc: p.5317 col.2 par.4), or the US3 enhancer in combination with a non-US3 minimal promoter (E/MIEm-CAT: p.5317 col.1 par.1). In other words, D1 discloses all technical features of claims 1-5,7-13,15,20 and 21, thereby depriving those of novelty.

2.2. It is considered that novelty of claims 1 and 9 could be established by restriction, on basis of e.g. p.6 ln.3, to such vectors encoding, instead of "a heterologous polypeptide", "an antigen derived from a pathogen" which is foreign with respect to the HCMV US3 protein.

3. INVENTIVE STEP (Art. 33(3) PCT)

3.1. The present application does not satisfy the criterion set forth in Article 33(3) PCT because the subject-matter of claim 6 does not involve an inventive step (Art.33(3) PCT and R.65(1)(2) PCT), for the following reasons: Document D1 can be considered to represent the most relevant state of the art for the subject-matter of present claim 6. Its teaching is as detailed in section 2.1

above. The difference in terms of technical features between the subject-matter of claim 6 and the closest prior art is the inclusion of HCMV Mie exon 1 after the transcription initiation sequence of the US3 promoter. The alleged technical effect is improvement in expression. The objective problem may therefore be regarded as providing improved US3-promoter-based constructs. The proposed solution is the inclusion of HCMV Mie exon 1 after the transcription initiation sequence of the US3 promoter. This solution cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons: D2 is one of several documents describing the advantageous effect of HCMV Mie exon 1 on heterologous gene expression. It is concluded that claim 6 proceeds of the mere juxtaposition of known technical features, each contributing their known technical effects, without producing any non-obvious working inter-relationship.

3.2. The present application is based on the observation that expression levels similar to those achieved with the Mie promoter can be achieved using the promoter of the HCMV US3 gene. Such is however only shown in the application with the so-called US3 and US3ex promoter constructs, i.e. with "US3 enhancer + US3 minimal promoter in absence of US3 silencer". These appear to be three essential technical features. In particular, it is noted that expression levels similar to those achieved with the Mie promoter are not shown to be achievable by the US3 enhancer combined with another minimal promoter (i.e. by present claim 9), nor in presence of R1 silencer (i.e. part of the scope of present claim 1). Claims 1-10 thus all lack essential technical feature(s), which is contrary to Article 6 PCT. It can even be objected that they do not meet the requirement of Art.33(3) PCT, since expression levels similar to those achieved with the Mie promoter cannot be considered to be achieved throughout the subject-matter of claims 1-10. Since these rely on claims 1-10, but do not include all essential technical features either, the same objection under Art.33(3) PCT applies to claims 11-23. These considerations would also apply to claims amended as suggested in section 2.2. above. Inclusion of all three essential technical features in the independent claims to the polynucleotide vectors would be warranted.

4. INDUSTRIAL APPLICABILITY (Art. 33(4) PCT)

4.1. For the assessment of present claim 19, and of claim 21 as far as it relates to a method practised in vivo, on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.